IN THE SPECIFICATION:

Please delete paragraph **[0008]** and replace it with the following paragraph:

[0008] At present the adenovirus serotype 5 is most widely used for gene therapy purposes. Similar to serotypes 2, 4 and 7, serotype 5 has a natural affiliation towards lung epithelia and other respiratory tissues. In contrast, it is known that, for instance, serotypes 40 and 41 have a natural affiliation towards the gastrointestinal tract. For a detailed overview of the disease association of the different adenovirus serotypes see ~~Table I~~ Table 1. In this ~~Table I~~ Table 1 there is one deviation from the literature. Sequence analysis and hemagglutination assays using erythrocytes from different species performed in our institute indicated that in contrast to the literature (De Jong et al. 1999) adenovirus 50 proved to be a D group vector whereas adenovirus 51 proved to be a B-group vector.

Please delete paragraph **[0015]** and replace it with the following paragraph:

[0015] The present invention solves the problem of how cartilage diseases can be counteracted by efficiently transducing a nucleic acid into primary chondrocytes. For that purpose, a gene delivery vehicle comprising a recombinant adenovirus having a tropism for primary human chondrocytes has been constructed. By a gene delivery vehicle is meant a carrier which can deliver at least one nucleic acid to a host cell. The nucleic acid that is delivered to a host cell may comprise a nucleic acid sequence encoding an amino acid sequence. The nucleic acid may further comprise at least one promoter, and/or enhancer, and/or terminator. It may also comprise transcription initiation sites, and the like. By delivering a nucleic acid to a host cell, the nucleic acid is moved from the outside to the inside of the host cell. Transient expression of the transgene is sufficient to trigger cells to form bone, or trigger angiogenesis. Therefore a non-integrating vector is preferred i.e. adenovirus. The present invention shows that primary human chondrocytes do not express detectable levels of CAR or MHC-class I, as is described in example 4. The latter indicates that it is difficult to transduce primary human chondrocytes with an adenovirus that enters the cells via these molecules, as for example the commonly-used

adenovirus serotype 5. One may use very high titers of the adenovirus, but this has several disadvantages such as a strong immune response caused by *de novo* synthesis of adenoviral genes that can subsequently by loaded in MHC class I complexes and presented to the immune system once the cells are transplanted in a host. To avoid toxic side effects, one would like to be able to transfer a nucleic acid to primary human chondrocytes by a gene delivery vehicle with high efficacy. High efficiency of infection allows for a reduction in the viral load that results in less virus binding to cells other than the target cells of interest. If the gene delivery vehicle infects too many other cells, the expression of the delivered nucleic acid in those other cells may cause many side effects. Therefore, the present invention discloses a gene delivery vehicle which has been made specific for a primary chondrocyte and which has the other properties of adenoviruses, for example not integrating its DNA in the host cell genome. To provide specificity for chondrocytes, the present invention discloses an adenovirus that comprises a deletion in the gene encoding for fiber protein that is replaced by a nucleic acid sequence encoding an amino acid sequence having a tropism for primary human chondrocytes. The nucleic acid sequence encoding an amino acid sequence having a tropism for primary human chondrocytes may be derived from any gene encoding for fiber protein. It may comprise at least one mutation that makes it different from any wild type gene encoding for fiber protein. Otherwise, the nucleic acid may be an unmodified gene encoding for fiber protein of any serotype. If the adenovirus disclosed in this invention comprises nucleic acid sequences of at least two different serotypes, the adenovirus is referred to as a chimeric ~~aderxovirus~~ adenovirus.

Please delete paragraph **[0017]** and replace it with the following paragraph:

[0017] In the counteraction of cartilage diseases, the nucleic acid which is delivered to primary human chondrocytes preferably either encodes an amino acid sequence that inhibits cartilage disease progression or a amino acid sequence that counteracts the loss of cartilage. The nucleic acid can encode a member of the family of bone ~~morphoqenesis~~ morphogenesis proteins. Alternatively, the nucleic acid can encode an amino acid sequence which provides the host cell with another wanted function.

Please delete paragraph **[0019]** and replace it with the following paragraph:

[0019] The initial step for successful infection is binding of adenovirus to its target cell, a process mediated through fiber protein. The fiber protein has a trimeric structure (Stouten et al. 1992) with different lengths depending on the virus serotype (Signas et al. 1985; Kidd et al. 1993). Different serotypes have polypeptides with structurally similar N and C termini, but different middle stem regions. N-terminally, the first 30 amino acids are involved in anchoring of the fiber to the penton base (Chrobcczek et al. 1995), especially the conserved FNPVYP (SEQ ID NO: 14) region in the tail (Arnberg et al. 1997). The knob is responsible for initial interaction with the cellular adenovirus receptor. After this initial binding secondary binding between the capsid penton base and cell-surface integrins is proposed to lead to internalization of viral particles in coated pits and endocytosis (Morgan et al. 1969; Svensson and Persson 1984; Varga et al. 1991; Greber et al. 1993; Wickham et al, 1993).

Please delete the section entitled SEQUENCE LISTING beginning on page 39 and ending on page 45 and replace it with the paper copy of the SEQUENCE LISTING included herewith.